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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/607,156	06/29/2000	Marcel Loetscher	2225.1001-009	8374

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EXAMINER	
MURPHY, JOSEPH F	
ART UNIT	PAPER NUMBER
1646	14

DATE MAILED: 04/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/607,156	Applicant(s) LOETSCHER ET AL.	
	Examin r Joseph F Murphy	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16,17,19-21 and 60-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *19-21,60,63,64,69-76 and 81-84* is/are allowed.

6)☒ Claim(s) *16-17, 61, 65-68, 77-78* is/are rejected.

7)☒ Claim(s) *62,79 and 80* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/15/2002 has been entered.

Formal Matters

Claims 16 and 61 were amended in Paper No. 10, 12/4/2001. Claims 16-17, 19-21, 60-84 are pending and under consideration.

Response to Amendment

The rejection of claims 63-64 under 35 USC § 112, first paragraph as not reasonably providing enablement for a variant having at least 90% amino acid sequence identity to SEQ ID NO: 2, has been withdrawn based on Applicant's arguments.

The rejection of claim 16 under 35 USC § 112, first paragraph has been obviated by Applicant's amendment, and is thus withdrawn.

The rejection of claim 16 under 35 USC § 112, first paragraph as not being enabled for a protein encoded by a nucleic acid which hybridizes to its own coding strand has been obviated by Applicant's amendment, and is thus withdrawn.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-17, 61, 65-68, 77-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The instant application does not disclose a representative number of cDNA's falling within the scope of the genus. In fact, only an amino acid with the sequence of SEQ ID NO: 2 is disclosed. Because the specification fails to describe more than a single species of the genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met. In the instant case there are a large number of nucleic acid sequences which share enough homology to hybridize to SEQ ID NO:1, however these sequences encode various unrelated proteins. Therefore, while the specification provides the necessary guidance to make the nucleic acid set forth in SEQ ID NO: 1, it does not provide the necessary guidance for one of skill in the art to make the nucleic acid sequences commensurate in scope with the claims.

The instant specification does not disclose structural features common to the members of the genus. As noted above, the disclosure of only one member of the claimed genus is insufficient to claim the entire group. See Id. at 1406. The only relevant identifying

characteristic disclosed in the specification is that the sequences must encode proteins with the appropriate biological activity. This is insufficient to support the generic claims

Applicant's attention is directed to Example 9 of the Written Description Guidelines. In Example 9, the genus nucleic acids meet the written description requirement because they were expressed and the encoded protein exhibited the function of binding to the dopamine receptor and stimulating adenylate cyclase activity. In the instant claims, a representative number of species are not disclosed because Applicant has only taught one species which binds IP-10 and Mig, not any other chemokine. The claims in the instant rejection recite the functional limitation that the encoded protein can bind one or more chemokines and can mediate cellular signaling and/or a cellular response thereto. The only amino acid specie provided is a receptor that binds IP-10 and Mig, not any other chemokines. In order for these claims to meet the written description requirement, in accordance with Example 9 of the written description guidelines, other species of nucleic acids which encode proteins which bind other chemokines would have had to have been disclosed. Therefore, the claims as written do not meet the written description requirement.

Claims 16-17, 61, 65-68, 77-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 2, does not reasonably provide enablement for a protein encoded by a

nucleic acid which hybridizes to SEQ ID NO: 1, for reasons of record set forth in Paper No. 8, 7/15/2001. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection of record set forth that the instant claims are overly broad in the recitation of "encoding a human CXCR3 protein" since no guidance is provided as to which of the polynucleotide species encoding the myriad of polypeptide species encompassed by the claim will retain the characteristics of a CXCR3 protein. In the specification (page 14, lines 5-35), Applicants disclose that variants of the polypeptide can be generated by mutagenesis, deletion or allelic variants, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of CXCR3. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape

characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a CXCR3 polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

(1) the breadth of the claims - The claims included in the instant rejection recite the functional limitation that the encoded protein can bind one or more chemokines and can mediate cellular signaling and/or a cellular response thereto.

(2) the nature of the invention - The instant invention is a protein.

(3) the state of the prior art - The Mikayama and Voet references demonstrate that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function.

(5) the level of predictability in the art - The Mikayama and Voet references demonstrate the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught one amino acid specie which binds IP-10 and Mig, not any other chemokine.

(7) the existence of working examples - Working examples are provided only for one amino acid specie which binds IP-10 and Mig, not any other chemokine.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 16-17, 61, 65-68, 77-78 in light of the

predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

The claims included in the instant rejection are overly broad in that the encoded protein can bind one or more chemokines and can mediate cellular signaling and/or a cellular response thereto. The only amino acid species provided in the disclosure encodes a receptor that binds IP-10 and MIG, not any other chemokines. Therefore, it would require undue experimentation for one of skill in the art to make and use the invention as claimed.

Conclusion

Claims 19-21, 60, 63-64, 69-76, 81-84 are allowable.

Claims 62, and 79-80 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 16-17, 61, 65-68, 77-78 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
April 1, 2002

DAVID S. ROMEO
PRIMARY EXAMINER